AR201-13781B

I. General Information

CAS Number: 763-69-9
Common Names: Propionic acid, 3-ethoxy-, ethyl ester
Ethyl 3-ethoxypropionate
Ethyl 3-ethoxypropionate
3-Ethoxypropionic acid ethyl ester
3-Ethoxypropionic acid ethyl ester
Ethoxypropionic acid, ethyl ester
Ethyl 3-ethoxypropanoate
Ethyl ester of 3-ethoxypropanoic acid
EEP

II. Physical-Chemical Data

A. Melting Point

Test Substance	
Test substance:	EEP
Remarks:	
Method	
Method:	Estimation
Remarks:	
Results	
Melting point value:	-26.92 °C
Remarks:	
References	MPBPWIN v1.40; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

B. Boiling Point

Test Substance	
Test substance:	EEP
Remarks:	
Method	
Method:	Estimation
Remarks:	Method was noted to have been an adaptation of Stein & Brown
Results	
Boiling point value:	170.88 °C
Remarks:	
References	MPBPWIN v1.40; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

C. Vapor Pressure

Test Substance	
Test substance:	EEP
Remarks:	
Method	
Method:	Estimation
Remarks:	Mean of Antoine and Grain methods
Results	
Vapor pressure value:	1.5 mmHg
Temperature:	25 ^{o}C
Remarks:	
References	MPBPWIN v1.40; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

D. Partition Coefficient

Test Substance	
Test substance:	EEP
Remarks:	
Method	
Method:	Estimation
Remarks:	
Results	
Log P_{OW}:	1.08
Remarks:	
References	KOWIN v1.66; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

E. Water Solubility

Test Substance	
Test substance:	EEP
Remarks:	
Method	
Method:	Estimation
Remarks:	
Results	
Value:	9,410 mg/L
Temperature:	25 ^{o}C
Description:	Slight (1-10 g/L)
Remarks:	A K_{ow} of 1.08 was used in the estimation
References	WSKOW v1.40; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

III. Environmental Fate Endpoints

A. Photodegradation

Test Substance	
Test substance:	EEP
Remarks:	
Method	
Method:	Estimation
Test type:	Atmospheric oxidation
Remarks:	
Results	
Temperature:	25 ^{o}C
Hydroxyl radicals reaction	
OH Rate constant:	15.8563 x 10^{-12} cm^3/molecule-sec
Half-life	0.675 Days (12-hr day; 1.5x10^6 OH/cm^3)
Ozone reaction:	No ozone reaction estimation was noted.
Remarks:	
Conclusions	Material is expected to rapidly degrade in the atmosphere.
References	AopWin v1.90; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

B. Stability in Water

Test Substance	
Test substance:	EEP
Remarks:	
Method	
Method:	Estimation
Test type:	Aqueous base/acid-catalyzed hydrolysis
Temperature:	25 ^{o}C
Remarks:	
Results	
Total K_b for pH >8:	7.802 x 10^{-2} L/mol-sec
Half-life (pH 8):	102.821 days
Half-life (pH 7):	2.815 years
Remarks:	Material is not readily hydrolyzed by water.
References	HYDROWIN v1.67; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

C. Biodegradation

Test Substance	
Test substance:	EEP
Remarks:	Purity >99%
Method	
Method:	OECD:TG-301B and Annex V C.4
Test type:	Ready biodegradation using the CO_2 evolution test (Modified Sturm)
GLP:	Yes
Year:	1996
Contact time:	28-days
Inoculum:	Activated sludge microorganisms (unacclimated)
Remarks:	Five inoculated carboys were used: 2 for the inoculum blank, one for a positive control (sodium benzoate), and two containing test article (tested at 34.8 mg/L; equivalent to 20 mg DOC/L). Microbe count was 10^6/ml.
Results	
Total degradation at test end:	60% and 66% (vessel 1 and vessel 2); loss of DOC was 99.9% in both vessels
Time for 10% degrad.:	7-days and 9-days (vessel 1 and vessel 2)
Does study meet 10-day window criteria:	No
Classification:	Results indicate material was not readily degraded.
Breakdown products:	Not determined
Remarks:	No significant amount of CO_2 was evolved from inoculum blank. Positive controls only reached 58% degradation by Day 14 and 70% by test end. As measured by DOC loss, the test substance was completely lost in 28-days. The contradiction between DOC loss and CO_2 evolution results may be due to the volatility of the test substance. The low CO_2 evolution does not necessarily mean the test substance is not degradable under environmental conditions, or after wastewater treatment.
Conclusions	
Data Quality	
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	Determination of Ready Biodegradability (Biotic Degradation) Using the CO_2 Evolution Test (Modified Sturm); Environmental Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Study No. EN-113-970309-A, August 21, 1996.

Other	The below comments are by Ms. Janice M. Beglinger, Biodegradation Area Coordinator Eastman Kodak Company, are to put perspective as to why results from the above summarized study differ from that of one conducted by Union Carbide (UC) summarized below using the same protocol (OECD 301B – Modified Sturm). After reviewing both studies the following findings were noted: 1. The amount of test chemical introduced was not the same. More test chemical was used in the Kodak (104.5 mg/3L) study than the UC (62.2 mg/3L) study. The Kodak study utilized a test concentration of 20 mg dissolved organic carbon/L. This was calculated using the molecular formula and weight of the compound. The UC study used 10 mg/L as organic carbon. The mg organic carbon was calculated using the analyzed value of the soluble organic carbon concentration of a 1000 mg/L stock solution. 2. The inoculum suspended solids (ss) concentrations differed. The Kodak test used 100 mL of inoculum at 24.7 mg/L ss per test vessel. The inoculum was prepared from mixed liquor supernatant. The UC study was inoculated to 30 mg/L ss with a bacterial seed suspension prepared from mixed liquor. The total volume used was not noted. It is possible that the combination of less chemical with a higher concentration of suspended solids would account for the difference between studies. 1. The inoculum itself could also account for a difference in overall degradation rates. Differences between bacterial populations could account for differences between laboratories, as they would not be homogenous. It is also possible that inoculum preparation procedures varied (between laboratories) as the OECD Guidelines allow for several variations. It should be noted that in addition to CO_2 evolution, the Kodak test also used dissolved organic carbon (DOC) analysis. DOC analysis is a direct measure, while CO_2 evolution is an indirect measure. At test end, loss of DOC for the Positive Control (sodium benzoate) was 99.8%. Loss of DOC for the test chemical was 99.9%. CO_2 evolution at test end for the Positive Control, Test vessel #1, and Test vessel #2 were 70%, 60%, and 66%, respectively. EEP was also the subject of a Zahn-Wellens study conducted at Kodak in 1995 (summarized below). The test was ended after 23 days resulting in 98% degradation. Test chemicals giving a result of greater than 20% loss of DOC in this test may be regarded as inherently biodegradable, whereas a result of greater than 70% loss of DOC is evidence of ultimate biodegradability. It should be noted that the inoculum was not acclimated for this study. In conclusion, test results of the UC study, DOC results from the Kodak study, and the 1995 Zahn-Wellens test conducted by Kodak, all indicate EEP Solvent may be classified as readily biodegradable.

Test Substance	
Test substance:	EEP
Remarks:	Purity unknown
Method	
Method:	OECD: TG-301B and OPPTS 835.3110
Test type:	Ready biodegradation using the CO_2 evolution test (Modified Sturm)
GLP:	Unknown
Year:	1997
Contact time:	28-Day
Inoculum:	Activated sludge microorganisms
Remarks:	Inoculum source was from the South Charleston, WV Wastewater Treatment Works, stock solution 1000 mg/L, stock DOC 482 mg/L, stock added/3L was 62.2 ml, product added/3L was 62.2 mg, carbon added 30.0 mg, test was completed in duplicate.
Results	
Total degradation at test end:	100% (Day 18)
Time for 10% degrad.:	<6 days
Does study meet 10-day window criteria:	Yes
Classification:	Results indicate material was readily biodegradable
Breakdown products:	Not determined
Remarks:	No significant amount of CO_2 was evolved from inoculum blank.
Conclusions	Material is readily degraded by wastewater microbes
Data Quality	
Remarks:	
References	Biodegradation testing of selected glycol ethers by carbon dioxide evolution test procedures; Union Carbide Corporation, September 24, 1998; File No.: 43290.
Other	

Test Substance	
Test substance:	EEP
Remarks:	Purity >99%
Method	
Method:	OECD: TG-302B
Test type:	Zahn-Wellens/EMPA test for inherent biodegradability
GLP:	Yes
Year:	1995
Contact time:	23-days
Inoculum:	Mixed-liquor suspended solids; unacclimated
Remarks:	Test article (50 mg DOC/L) and positive control were run in duplicate using 2L Erlenmeyer flask. Another flask was used as a blank control. Test solutions were agitated with magnetic stir bars and protected from light by aluminum foil. Dissolved oxygen, pH, and DOC analysis were determined on days 1, 3, 6, 8, 10, 14, 17, and 23.
Results	
Degradation %:	98% decrease in DOC (Day 23)
Time for 10% degrad.:	< 1-day
Classification:	Material is inherently biodegradable under the definition of this test.
Breakdown products:	Not determined
Remarks:	Positive control had a DOC removal exceeding 70% within 14-days. This fulfills the requirements of a valid test. No protocol deviations were noted.
Conclusions	Results indicate material would not be expected to be persistent in the environment. Test article does not require any European Union labeling statement relating to long-term effects.
Data Quality	
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	Determination of Inherent Biodegradability (Biotic Degradation) Using the Zahn/Wellens/EMPA Test; Environmental Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Study No. EN-111-970309-1, April 17, 1996.
Other	

Test Substance	
Test substance:	EEP
Remarks:	Purity >99%
Method	
Method:	OECD: TG-301E and EEC/Annex V Guideline C.3
Test type:	Ready Biodegradability
GLP:	Yes
Year:	1991
Contact time:	28-days
Inoculum:	Unacclimated microorganisms from secondary wastewater effluent
Remarks:	Test article was evaluated in duplicate with results averaged. The concentration of DOC (Day 0: 21.5 mg/L) was determined for each vessel on Days 0, 7, 14, 21, 27, and 28. Sterile chemical control DOC was analyzed at the start and on Day 28. Dissolved oxygen and pH were assessed at time 0 and on Day 28. A positive control of Sodium benzoate was used to validate the test system. Another flask was used as a blank control. All test flasks were oscillated (100 rpm) in the dark at a temperature of 20-25 ^{o}C.
Results	
Degradation %:	43% decrease in DOC (Day 28)
Time for 10% degrad.:	< 7-Days
Classification:	Material is moderately biodegradable under the definition of this test.
Breakdown products:	Not determined
Remarks:	Positive control had a DOC removal exceeding 90% at Day 7. This fulfills the requirements of a valid test. No protocol deviations were noted.
Conclusions	Under condition of this assay the material appears to have a moderate potential to be degraded in the environment
Data Quality	
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Study No. EN-102-906315-1, June 17, 1991.
Other	

D. Transport between Environmental Compartments (Fugacity)

Test Substance	
Test substance:	EEP
Remarks:	
Method	
Test type:	Estimation
Model used:	Level III Fugacity Model; EPIWIN:EQC from Syracuse Research Corporation
Remarks:	
Results	
Model data and results:	
Estimated distribution and media concentration (levels II/III):	Concentration (%) Air 1.59 Water 50.5 Soil 47.8 Sediment 0.093
Remarks:	Physical chemical values utilized in this model were default values obtained from the EPIWIN program.
Data Quality	
Remarks:	
References	Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210. The Level III model incorporated into EPIWIN is a Syracuse Research Corporation adaptation of the methodology described by Mackay *et al.* 1996; *Environ. Toxicol. Chem.* 15(9), 1618-1626 and *Environ. Toxicol. Chem.* 15(9), 1627-1637.
Other	

IV. Ecotoxicity

A. Acute Toxicity to Fish

Test Substance	
Test substance:	EEP
Remarks:	Purity was >99%
Method	
Method:	OECG:TG-203 and EEC/Annex V C.1.
Test type:	Acute lethality
GLP:	Yes
Year:	1994
Species/strain:	Fathead minnow (*Pimephales promelas*)
Analytical monitoring:	Yes; Exposure solutions, temperature, pH, dissolved oxygen
Exposure period:	96-Hour; static
Remarks:	Study was conducted in duplicate with 10 fish/concentration with a loading rate of < 1 g/L. The photoperiod consisted of 16-hours on and 8-hours off with a 20-minute transition period.
Results	
Observations on precipitation:	No precipitation was noted. However, although the water was initially clear, test tanks became cloudy at 72-hours at exposure levels of 34.5 and 61.5 mg/L (replicates A and B) and at 111 mg/L in replicate B. By 96-hours, the two lower levels became slightly cloudy. Interestingly, cloudiness was not reported at the highest concentration level or at 111 mg/L in replicate A.
Nominal concentration:	10.5, 19, 34.5, 61.5, 111, 200 mg/L
Measured concentration:	Test A: 9.5, 13.2, 25.4, 46.4, 100.1, 174.0 mg/L Test B: 9.4, 13.4, 23.8, 44.2, 83.2, 174.4 mg/L
Endpoint value:	Test A: LC_{50} 55.3 mg/L; NOEC 25.4 mg/L Test B: LC_{50} 45.3 mg/L; NOEC 23.8 mg/L
Biological observations:	Normal behavior and appearance was noted in all fish at all time points exposed to 34.5 mg/L and below. Deaths and decreased activity were noted in a dose-dependent manner at levels of 61.5 and above.
Statistical methods:	LC_{50} calculations were determined by: (1) Stephan, C.E. 1977. Methods for Calculating an LC_{50}. In: F.L. Mayer and J.L. Hamelink, Eds., Aquatic Toxicology and Hazard Evaluation, Spec. Tech. Publ. No. 634, ASTM, Philadelphia, PA, pp. 65-84. (2) American Society for Testing and Materials. 1988. Proposed New Standard Practice for Using Probit Analysis. ASTM E-47.07. Draft#4. June, 1988.
Remarks:	No significant protocol deviations were noted. Water temp remained at 20 +/- 1 ^{o}C, The extremes for pH ranged from 7.48 to 8.48 and dissolved oxygen ranged from 5.1 – 9.0 mg/L.
Conclusions	The 96-hour LC_{50} value indicates that the test substance would be assigned the risk phrase “harmful to aquatic organisms” according to the European Union’s labeling directive and would correspond to a “moderate concern level” according to the U.S. EPA’s assessment criteria.

Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	An Acute Aquatic Effects Test with the Fathead Minnow; Environmental Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Study No. EN-430-970309-l, July 7, 1995.
Other	Data from a study completed by the Union Carbide Company using similar methodologies indicated the 96-hour LC50 was 90 mg/L and the NOEC was 62.5 mg/L. These values are very comparable to what is summarized above.

B. Acute Toxicity to Aquatic Invertebrates

Test Substance	
Test substance:	EEP
Remarks:	Purity was >99%
Method	
Method:	OECD: TG-202 and EEC/Annex V C.2
Test type:	Acute immobilization
GLP:	Yes
Year:	1994
Species/strain:	*Daphnia magna*
Analytical procedures:	Aliquots of exposure solution were submitted for concentration determinations at 0 and 48 hours. Temperature, dissolved oxygen, and pH were also determined at these same time periods.
Test details:	48-hour exposure period; static
Remarks:	Study was conducted in duplicate
Results	
Nominal concentration:	95.0, 171.5, 308.5, 555.5, and 1000 mg/L
Measured concentration:	Test A: 70.2, 133.1, 245.7, 479.7, and 911.1 mg/L Test B: 67.2, 136.1, 260.9, 461.4, 918.7 mg/L
Endpoint value:	Test A(48 hr): EC_{50} >479.7 mg/L; NOEC 479.7 mg/L Test B(48 hr): EC_{50} 785.0 mg/L; NOEC 461.4 mg/L
Biological observations:	Daphnids exhibited behavior comparable to controls at a test concentration of 555.5 mg/L and below. Depressed activity and immobilization was noted only at the 1000 mg/L level and primarily at the 24 hour and 48 hour observation periods.
Statistical methods:	LC_{50} calculations were determined by: (1) Stephan, C.E. 1977. Methods for Calculating an LC_{50}. In: F.L. Mayer and J.L. Hamelink, Eds., Aquatic Toxicology and Hazard Evaluation, Spec. Tech. Publ. No. 634, ASTM, Philadelphia, PA, pp. 65-84. (2) American Society for Testing and Materials. 1988. Proposed New Standard Practice for Using Probit Analysis. ASTM E-47.07. Draft#4. June, 1988.
Remarks:	Minor protocol deviations were noted. However, they were either deemed as insignificant and would not have affected study outcome, or their impact would have actually lead to more conservative final values. Water temp remained at 19 ^{o}C, The extremes for pH ranged from 7.7 to 8.1 and dissolved oxygen ranged from 7.6 – 9.2 mg/L.
Conclusions	The 48-hour EC_{50} value indicates that the test substance would not require any labeling pertaining aquatic toxicity according to the European Union's labeling directive and would correspond to a "low concern level" according to the U.S. EPA's assessment criteria.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	An Acute Aquatic Effects Test with the Daphnid; Environmental Sciences Section, Health and Environment Laboratories, at Eastman Kodak Company, Rochester, NY; Study No. EN-431-970309-1; July 25, 1995.
Other	

C. Toxicity to Aquatic Plants

Test Substance	
Test substance:	EEP
Remarks:	Purity was >99%
Method	
Method:	OECD: TG-201 and EEC/Annex V C.3
Test type:	Growth inhibition limit test with the alga
GLP:	Yes
Year:	2000
Species/strain:	*Selenastrum capricornutum*
Endpoint basis:	Cell concentrations (biomass) and growth rate
Exposure period:	72-hours, static
Analytical procedures:	Temperature, light intensity, rpm, and test substance concentration were assessed at the 0, 24, 48, and 72 hours. The pH was assessed at time 0 and after 72 hours.
Remarks:	The concentration of algae was set at 10^4 cells/ml.
Results	
Nominal concentration:	120 mg/L
Measured concentration:	118.82 mg/L 0 hours and 114.86 mg/L (geometric mean concentration over the 3 days)
Endpoint value:	The estimated E_bC_{50} and E_rC_{50} were not determined as there was no effect on algae growth.
NOEC:	>114.86 mg/L (72 hr)
Biological observations:	No deformed cells were noted
Was control response satisfactory:	Yes (culture concentrations increased by a factor of 72-fold)
Statistical methods:	NA (no effects were seen at highest exposure concentration)
Remarks:	A mean illumination of 754 +/- 13.7 foot-candles was maintained. The mean temperature was 24°C and pH ranged from 7.4 to 7.9. Cultures were oscillated at 100 rpm. There was a 7.2% loss of test material over the 72-hour period.
Conclusions	The 72-hour E_bC_{50} and E_rC_{50} values indicate that, based on this study, the test substance would not be classified as "harmful to aquatic organisms" according to the European Union's labeling directive and would be classified in a "low concern" category according to the U.S. EPA's assessment criteria.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD-study conducted under GLP assurances
References	A Growth Inhibition Test with the Alga, *Selenastrum capricornutum*; Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Study No. EN-512-906315-A, January 30, 2001.
Other	

V. Toxicological Data

A. Acute Toxicity

Test Substance	
Test substance:	EEP
Remarks:	Purity 99.9%
Method	
Method:	Acute toxicity; OECD: TG-401 (dated May 12, 1981)
Test type:	LD_{50} estimate
GLP:	Yes
Year:	1986
Species/strain:	Rat/CRL:CD (SD)
Sex:	Male and Female
Animals/sex/dose:	5
Vehicle:	None
Route of exposure:	Oral
Remarks:	Only a single dose of 5,000 mg/kg was utilized; study also included histopathology on many tissues including those of the central nervous system.
Results	
Value:	LD_{50}>5,000 mg/kg males LD_{50} 3200-5,000 mg/kg females
Deaths at each dose:	No males died; 3 females died (2 on Day 1 and one on Day 2)
Remarks:	Males: All demonstrated slight weakness and ataxia on Day 1 after dosing. On Day 2, and subsequent days, no abnormal clinical sign were noted, and all had normal weight gains. Females: No abnormal clinical signs were observed on the day of dosing. The next day, 2 animals were found dead and the remaining three exhibited signs of moderate to severe weakness and ataxia. A third animal died during the night between Days 1 and 2. On Day 2 the remaining animals had slight weakness, but were clinically normal on all subsequent days and demonstrated normal weight gain. The cause of death of the three females was not evident. There were no test article induced changes in any of several organs and tissues removed from the seven rats that survived till experimental termination. There was no evidence of neurotoxicity based on an absence of lesions in the brain, spinal cord, peripheral nerves, dorsal root ganglia, skeletal muscle, and neural tissue present in visceral organs. The LD_{50} range listed for females is from 3200 – 5000 mg/kg based on the results of another study (not reported) in which no females died following an acute oral exposure of 3,200 mg/kg.
Conclusions	Material is considered slightly toxic
Data Quality	
Reliability:	Reliable without restriction
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	Acute oral toxicity study of ethyl-3-ethoxypropionate; Eastman Kodak Company, Rochester, NY; HAEL No.: 85-0044; June 26, 1986.
Other	Supplemental data from a study completed by the Union Carbide Company indicated the oral LD_{50} for male rats was 6.63 ml/kg and 5.41 ml/kg for females. (UCAR Ester EEP acute toxicity and primary irritancy studies Bushy Run Research Center; Project report 50-84; June 5 1987.)

Test Substance	
Test substance:	EEP
Remarks:	99.8%
Method	
Method:	Acute toxicity; Other
Test type:	LC_{50} estimate
GLP:	Yes
Year:	1983
Species/strain:	Rat/COBS:CD(SD)BR
Sex:	Male
Animals/sex/dose:	4/dose
Vehicle:	None
Route of exposure:	Inhalation
Remarks:	Rats were exposed in 20-L glass bell jars for a single 6-hour period to 0, 500 or 1000 ppm (actual levels were 481 and 998 ppm) EEP as a vapor. They were subsequently held for 14-days for observation and weight gain analysis. Test material air concentration and temperature within the chamber was quantified hourly. Gross pathologic examinations were conducted at study termination.
Results	
Value:	
Deaths at each dose:	LC_{50}>998 ppm; 5,967 mg/m^3 (males)
Remarks:	There were no deaths at any exposure level Body weight gain was comparable to controls. Clinical signs consisted of minimal (500 ppm) and minor (1000 ppm) lethargy and decreased aural investigatory reflex (both groups) during exposure. Animals were void of any gross lesions at terminal necropsy.
Conclusions	
Data Quality	
Reliability:	
Remarks:	Reliable without restriction This was a well-documented OECD-like guideline study conducted under GLP assurances.
References	
	LC_{50} inhalation study of compound ethyl-3-ethoxypropionate; Toxicological Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; HS&HFL No. 83-0169; December 9, 1983.
Other	

B. Repeated Dose Toxicity

Test Substance	
Test substance:	EEP
Remarks:	Purity was 99.9%
Method	
Method:	OECD: TG-407
Test type:	Repeated oral-dose toxicity
GLP:	Yes
Year:	1986
Species/strain:	Rat/CRL:CD(SD)
Route of exposure:	Oral intubation
Duration of test:	28-Days
Dose levels:	0, 100, 1000 mg/kg
Sex:	Male and Female; 5/dose level
Exposure period:	Single daily gavage
Frequency of treatment:	5 days/week
Control group and treatment:	Yes; Distilled water
Post-exposure observation period:	None
Remarks:	Due to gavage error-induced deaths, 2 animals in the high-dose group were replaced with animals of comparable age and weight on Day 3.
Results	
NOAEL (NOEL):	100 mg/kg NOEL
Toxic responses by dose:	There was no test material-induced mortality or clinical signs. Weight gain and feed intake were also not significantly impacted by test article. There were no alterations in the hematological parameters assessed and organ weights, nor were any lesions noted after gross or microscopic examination. The only effect noted in this study were an increase in serum enzymes (AST and SDH) and creatinine levels in animals receiving 1000 mg/kg.
Statistical methods:	One-way ANOVA, Bartlett's test, and Duncan's multiple range test using a p value of <0.05 to indicate statistical significance.
Remarks:	
Conclusions	Material was well tolerated with minor effects noted on liver enzymes and creatinine levels not accompanied by alterations in morphological appearance of any organ examined.
Data Quality	
Reliability:	Reliable with restriction
Remarks:	Although this was an OECD guideline study conducted under GLP assurances, the study report was somewhat lacking in detail.
References	Four-Week Oral Toxicity Study of Ethyl-3-Ethoxypropionate in the Rat; Toxicological Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Study No.: 850044G3; March 16, 1986.
Other	

Test Substance	
Test substance:	EEP
Remarks:	Purity was >99%
Method	
Method:	Methods were comparable to OECD: TG-413
Test type:	Subchronic inhalation toxicity
GLP:	Yes
Year:	1986
Species/strain:	Rat/CRL:CD(SD)BR
Route of exposure:	Inhalation
Duration of test:	90-Days
Dose levels:	0, 250, 500, 1000 ppm
Sex:	Male and female; 15/dose level
Exposure period:	6 hours/day
Frequency of treatment:	5 days/week
Control group and treatment:	Controls exposed to filtered room air and were otherwise treated similarly
Post-exposure observation period:	None
Remarks:	Test atmosphere was in vapor form
Results	
NOAEL (NOEL):	250 ppm; 1,495 mg/m^3
Actual doses received:	0, 251, 510, 996 ppm
Toxic responses by dose:	One female exposed to 1000 ppm died on day 54. The cause was not determined due to autolysis. Body weight: Statistically significant decreases in body weight at termination were noted in mid- and high-dose animals of both sexes. Clinical signs: The only major observation noted was signs of irritation manifested as lacrimation, sialorrhea, red or brown discoloration of facial hair, and unkempt appearance. The severity was noted to be minimal and was seen in both sexes. Lethargy was noted in high-dose animals and only occurred during the first few exposures. Hematology: The only effect noted was a slight increase (biologically insignificant) in lymphocyte percentage in high-dose females. Clinical chemistry: High-dose males had a slight, but statistically significant, decrease in serum glucose and increase in creatinine level. High-dose females also showed this effect in creatinine. Additional test-article related changes in females consisted of a dose responsive increase in alkaline phosphatase (significant at 500 and 1000 ppm). Organ effects: There were no statistically significant changes in organ weights or any histopathological changes to suggest a test article-induced toxicity.
Statistical methods:	One-way ANOVA, Bartlett's test, and Duncan's multiple range test using a p value of <0.05 to indicate statistical significance.
Remarks:	
Conclusions	

Data Quality	
Reliability:	Reliable without restriction
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	90-Day Inhalation Toxicity Study of Ethyl-3-Ethoxypropionate in the Rat; Toxicological Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Experiment No.: 850044I1; June 30, 1986.
Other	

C. Genetic Toxicity - Mutation

Test Substance	
Test substance:	EEP
Remarks:	Purity was 99.8%
Method	
Method:	Other; OECD: TG-471-like
Test type:	*In vitro* mutagenicity
GLP:	Yes
Year:	1986
Species/strain:	*Salmonella typhimurium* (strains: TA98, 100, 1535, 1537, and 1538)
Metabolic activation:	Yes; rat liver S9
Concentration tested:	Maximum concentration tested was 15000 ug/plate
Remarks:	Positive controls (2-aminoanthracene, sodium azide, 9-aminoacridine, picrolonic acid, and ICR-191) were run concurrently. Negative control was the test vehicle dimethylsulfoxide. The test article was plated in triplicate. A chemical is considered positive when all criteria are met and there is a reproducible dose-response relationship that exceeds 10^3 revertants/nanomole.
Results	
Result:	No positive responses were induced by EEP in any of the tester strains
Cytotoxic concentration:	Cytotoxicity began at 3164 ug/plate and showed a 26% decrease at 10,000 ug/plate (-S9) and a 16% decrease with S9 activation.
Precipitation concentration:	No precipitate was observed at maximum concentration tested.
Genotoxic effects	
With activation:	Negative
Without activation:	Negative
Statistical methods:	Means and standard deviations were determined for each of the dosing regimens; then each mean was assessed for significance using Student's t-test. Further statistical analyses were outlined but were not needed due to the absence of an increase in the number of revertants colonies at any dose beyond the positive control.
Conclusions	Material was not genotoxic under conditions of this assay.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD-like guideline study conducted under GLP assurances.
References	Evaluation of Ethyl-3-Ethoxypropionate in the Salmonella/Microsome Mutagenicity Assay; Toxicological Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; HAEL No.: 83-0169; January 26, 1986.
Other	

D. Genetic Toxicity – Chromosomal Aberrations

Test Substance	
Test substance:	EEP
Remarks:	Purity was >99%
Method	
Method:	OECD: TG-473
Test type:	Aberration assay in CHO cells
GLP:	Yes
Year:	2000
Species/strain:	Chinese hamster ovary cells
Route of exposure:	*In vitro*
Concentration tested:	Up to 1500 ug/ml (this is >10 mM, the assay maximum)
Metabolic activation:	Yes; Aroclor 1254 induced rat liver S9
Remarks:	Positive controls consisted of Mitomycin C (-S9) and cyclophosphamide (+S9). 200 cells per concentration were evaluated and each concentration had two replicates.
Results	
Result:	No significant increases in cells with chromosomal aberrations, polyploidy, or endoreduplication were observed.
Cytotoxic concentration:	>1500 mg/ml, the maximum dose tested
Precipitation concentration:	No precipitate was observed at maximum concentration tested.
Genotoxic effects	
With activation:	Negative
Without activation:	Negative
Statistical methods:	Statistical analysis employed a Cochran-Armitage test for linear trends and Fisher's Exact Test to compare the percentage of cells with aberrations.
Remarks:	
Conclusions	Material was not genotoxic under conditions of this assay.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	Chromosomal Aberrations in Chinese Hamster Ovary (CHO) cells with EC2000-0201, EEP; Covance Laboratories Inc., Vienna, VA; Study number: 21202-0-437OECD; April 6, 2000.
Other	

E. Developmental Toxicity

Test Substance	
Test substance:	EEP
Remarks:	Purity was 99.7%
Method	
Method:	This study essentially followed current OECD: TG-414 guidelines
GLP:	Yes
Year:	1983/1984
Species/strain:	Rat/COBS:CD(SD)BR
Sex:	Females; 25/exposure level
Route of exposure:	Inhalation
Exposure levels:	0, 125, 250, 500, 1000 ppm
Actual exposure levels:	0, 123, 245, 500, 975 ppm
Exposure period:	6 hours/day
Frequency of treatment:	Days 6-15 of gestation
Control group and treatment:	Filtered room air
Remarks:	Groups of 45-day old males and females were housed 1:1 over a four-day mating period. Animals were exposed to test article as a vapor on days 6-15 of gestation using whole-body inhalation chambers. Exposure conditions were well monitored. Maternal body weight and food consumption was monitored regularly. All dams were monitored daily (except weekends) for behavioral changes. On Day 20 dams were euthanized by CO_2. Hematological and clinical chemistry analyses were conducted on 10 randomly chosen animals. The uterine horns were removed and implantation sites examined. Ovaries were examined and corpora lutea quantified. A gross examination was conducted on the visceral and thoracic cavities and the liver, kidneys, spleen, and thymus were weighed and microscopically examined. A section of the femur and mesenteric lymph nodes were also removed for histological examination. Viable fetuses were removed, weighed, sexed, and examined for gross abnormalities. They were divided in two and fixed appropriately for either internal soft tissue examinations or for skeletal defects.
Results	
Maternal toxicity NOEL:	125 ppm, 747 mg/m^3
NOEL for teratogenicity:	1000 ppm; 5,979 mg/m^3
NOEL for fetotoxicity:	500 ppm; 2,990 mg/m^3
Maternal toxic responses by dose:	Absolute body weights were lower in dams exposed to 500 and 1000 ppm during gestation days 6-16, while terminal (Day 19) weights were comparable to control. While maternal weight gain and food consumption during Days 6-16 were significantly lower at exposure levels of 250 ppm and higher. Clinical signs of toxicity were only noted in the 1000 ppm group and consisted of lethargy, salivation, and reddish discoloration of facial hair. There were no significant effects seen in the hematological parameters, clinical chemistries, or visceral organs weighed or microscopically examined.

Fetal toxic responses by dose:	No differences were noted in any of the reproductive indices, or in fetal body weight or sex ratios. External, internal soft tissue and skeletal examinations of the fetuses revealed no treatment-related major malformations in any exposed groups. Slight increases in the incidence of some minor internal soft tissue alterations and skeletal variants indicative of slight fetotoxicity were seen in litters exposed to 1000 ppm. The appearance of rudimentary thoracolumbar ribs (14^{th}) was also increased in litters exposed to 1000 ppm.
Statistical methods:	Continuous data were analyzed using a one-way ANOVA and Duncan's Multiple Range test. Homogeneity of variance was tested by Bartlett's test. Incidence data were compared using Chi-square contingency tables and each test group was compared to control using Fisher's Exact Test.
Remarks:	
Conclusions	It was concluded that EEP was not teratogenic. While slight evidence of fetotoxicity was noted, this occurred at levels that induced significant maternal toxicity (1000 ppm).
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD-like study conducted under GLP assurances
References	The Developmental Toxicity of Ethyl-3-Ethoxypropionate in the Rat; Toxicological Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Study: 83-0169-2; June 25, 1984.
Other	

Test Substance	
Test substance:	EEP
Remarks:	Purity was 99.9%
Method	
Method:	"New and Revised Health Effects Test Guideline" EPA 560/6-84-002 and was also conducted in general agreement with that for an "Inhalation Developmental Toxicity Study" (HG-Organ/Tissue-Dev Tox-Inhal, October 1984).
GLP:	Yes
Year:	1986
Species/strain:	Rabbit/New Zealand White
Sex:	Female; 18/exposure level
Route of exposure:	Inhalation
Exposure levels:	0, 125, 250, 500, 1000 ppm
Actual exposure levels:	0, 124, 247, 498, 997 ppm
Exposure period:	6 hours/day
Frequency of treatment:	Days 6-18 of gestation
Control group and treatment:	Filtered room air
Remarks:	The methodology followed in this study is essentially identical to that of OECD: TG-414 guidelines. The liver, kidneys, spleen, and thymus were weighed and microscopically examined. A section of the femur and mesenteric lymph nodes, along with any gross lesions were also removed for histological examination. Test atmosphere was in vapor form.
Results	
Maternal toxicity NOAEL:	125 ppm; 747 mg/m^3
Developmental toxicity NOAEL:	1000 ppm; 5,979 mg/m^3
Maternal toxic responses by dose:	No mortalities were noted. Pregnancy rates and the incidence of pregnancies lost to abortion or premature delivery were comparable between all groups. No adverse effects due to treatment were noted in maternal hematology, clinical chemistry data, organ weights, or in organs examined grossly or microscopically. A reduction in food consumption was seen on Days 6 and 7 at 250 and 500, and 1000 ppm. Several females at 500 and 1000 ppm were reported to have excessive lacrimation on the first day of exposure. Excessive salivation on the first day of exposure was also noted at 1000 ppm. Decreased body weight gain was noted for Days 6-9 and 6-18 in animals exposed to 1000 ppm.
Fetal toxic responses by dose:	No treatment-related external, internal soft tissue, or skeletal anomalies were seen at any exposure concentration in the harvested fetuses.
Statistical methods:	Homogeneity of variance was tested by Bartlett's test followed by parametric or non-parametric procedures if variances were equal or not respectively. Parametric data were analyzed using a one-way ANOVA followed by either Dunnett's test. Non-parametric results utilized Kruskal-Wallis test and a summed rank test (Dunn) to determine which treatment differed from control. A test for trend in dose levels was also performed with standard regression (parametric data) or Jonckheere's test in the non-parametric cases. All ratios were transformed via the arc sine transformation prior to analysis. Incidence data were compared using Chi-square contingency tables and each test group was compared to control using Fisher's Exact test. The significance level was corrected via the Bonferroni inequality to assure an overall test of the stated significance level. Thirdly, Armitage's test for linear trend in the dosage groups was performed.

Remarks:	
Conclusions	It was concluded that EEP was not teratogenic or fetotoxic. Slight evidence of maternal toxicity was noted at 1000 ppm.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD-like guideline study conducted under GLP assurances.
References	An Inhalation Developmental Toxicity Study in Rabbits with Ethyl-3-Ethoxypropionate; Bio/Dynamics Inc. East Millstone, NJ; Project No.: 86-3035; March 17, 1987.
Other	

F. Toxicity to Reproduction

Test Substance	
Test substance:	EEP
Remarks:	Purity was >99%
Method	
Method:	Methods were comparable to OECD: TG-413
Test type:	Subchronic inhalation toxicity
GLP:	Yes
Year:	1986
Species/strain:	Rat/CRL:CD(SD)BR
Route of exposure:	Inhalation
Duration of test:	90-Days
Exposure levels:	0, 250, 500, 1000 ppm
Sex:	Male and female; 15/exposure level
Exposure period:	6 hours/day
Frequency of treatment:	5 days/week
Control group and treatment:	Controls exposed to filtered room air and were otherwise treated similarly
Post-exposure observation period:	None
Remarks:	Testes and ovaries were weighed at time of necropsy. Testes, epididymides, male accessory sex gland, ovaries, vagina, uterus, and fallopian tubes were examined microscopically. Test atmosphere was in vapor form.
Results	
NOAEL:	>1000 ppm; 5,979 mg/m^3
Actual exposure levels:	0, 251, 510, 996 ppm
Toxic responses by dose:	There were no statistically significant changes in any of the weighed reproductive organs, nor were there any histopathological changes in any reproductive organs examined.
Statistical methods:	One-way ANOVA, Bartlett's test, and Duncan's multiple range test using a p value of <0.05 to indicate statistical significance.
Remarks:	
Conclusions	No evidence of toxicity to the reproductive organs was noted.
Data Quality	
Reliability:	Reliable with restriction
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances. The study only assessed reproductive organ weight and histology.
References	90-Day Inhalation Toxicity Study of Ethyl-3-Ethoxypropionate in the Rat; Toxicological Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Experiment No.: 850044I1; June 30, 1986.
Other	